

WHAT IS CLAIMED IS:

1. An isolated peptide selected from the group consisting of:

5 (a) a peptide set forth in Table 1 or Table 2 and

(b) a derivative of the peptide in (a).

2. The isolated peptide of claim 1, wherein Xaa₁ is Glu, Xaa₂ is pyro-Glu, Xaa₄ is Trp and Xaa₅ is Tyr.

10 3. The derivative of the peptide of claim 1, in which the Arg residues may be substituted by Lys, ornithine, homoarginine, nor-Lys, N-methyl-Lys, N,N,N-trimethyl-Lys or any synthetic basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoarginine, nor-Lys, or any synthetic basic amino acid; the Tyr residues may be substituted with meta-Tyr, ortho-Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any synthetic hydroxy containing amino acid; the Ser residues may be substituted with Thr or any synthetic hydroxylated amino acid; the Thr residues may be substituted with Ser or any synthetic hydroxylated amino acid; the Phe residues may be substituted with any synthetic aromatic amino acid; the Trp residues may be substituted with Trp (D), neo-Trp, halo-Trp (D or L) or any aromatic synthetic amino acid; the Asn, Ser, Thr or Hyp residues may be glycosylated; the Tyr residues may also be substituted with the 3-hydroxyl or 2-hydroxyl isomers (meta-Tyr or ortho-Tyr, respectively) and corresponding O-sulpho- and O-phospho-derivatives; the acidic amino acid residues may be substituted with any synthetic acidic amino acid, e.g., tetrazolyl derivatives of Gly and Ala; the aliphatic amino acids may be substituted by synthetic derivatives bearing non-natural aliphatic branched or linear side chains C_nH_{2n+2} up to and including n=8; the Met residues may be substituted by Nle; the Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L); pairs of Cys residues may be replaced pairwise with isoteric lactam or ester-thioether replacements, such as Ser/(Glu or Asp), Lys/(Glu or Asp), Cys/Glu (or Asp) or Cys/Ala combinations; and the peptide may be radioiodinated or radiotriated.

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4. A substantially pure μ -conotoxin peptide derivative comprising a permutant of the peptide of claim 1.

5. A substantially pure μ -conotoxin peptide derivative comprising the peptide or peptide derivative of claim 1 modified to contain an O-glycan, an S-glycan or an N-glycan.

6. A substantially pure μ -conotoxin peptide derivative comprising the peptide derivative of claim 4 modified to contain an O-glycan, an S-glycan or an N-glycan.

10 7. An isolated nucleic acid encoding a μ -conopeptide propeptide having an amino acid sequence set forth in Table 1.

15 8. The isolated nucleic acid of claim 7, wherein the nucleic acid comprises a nucleotide sequence set forth in Table 1.

9. An isolated μ -conopeptide propeptide having an amino acid sequence set forth in Table 1.

20 10. A method for treating or preventing disorders associated with voltage gated ion channel disorders in which comprises administering to a patient in need thereof a therapeutically effective amount of a peptide of claim 1 or a pharmaceutically acceptable salt thereof.

11. The method of claim 10, wherein said disorder is a neurologic disorder.

25 12. The method of claim 11, wherein said neurologic disorder is Amyotrophic Lateral Sclerosis.

13. The method of claim 11, wherein said neurologic disorder is head trauma.

30 14. The method of claim 11, wherein said neurologic disorder is epilepsy.

15. The method of claim 11, wherein said neurologic disorder is a neurotoxic injury
associated with conditions of hypoxia, anoxia or ischemia.

5 16. The method of claim 15, wherein said neurotoxic injury is associated with stroke,
cerebrovascular accident, brain or spinal cord trauma, myocardial infarct, physical
trauma, drownings, suffocation, perinatal asphyxia, or hypoglycemic events.

10 17. The method of claim 10, wherein said disorder is pain.

18. The method of claim 17, wherein said pain is migraine, acute pain, persistent pain,
chronic pain, neuropathic pain or nociceptive pain.

19. The method of claim 18, wherein the pain is trigeminal neuralgia, diabetic neuropathy,
post-herpetic neuralgia, neuroma pain, phantom limb pain.

20 20. The method of claim 17, wherein said pain is burn pain.

21. The method of claim 10, wherein said disorder is a neuromuscular disorder.

20 22. The method of claim 21, wherein said neuromuscular disorder is myofacial pain
syndrome, chronic muscle spasm, dystonias or spasticity.

25 23. A method for providing musculoskeletal relaxation in a patient undergoing a surgical
procedure requiring anesthesia which comprises administering to a patient in need
thereof a therapeutically effective amount of a peptide of claim 1 or a pharmaceutically
acceptable salt thereof.

24. A method of alleviating pain which comprises administering to a mammal that is either
exhibiting pain or is about to be subjected to a pain-causing event a pain-alleviating
amount of a peptide of claim 1 or a pharmaceutically acceptable salt thereof.

30 25. The method of claim 24, wherein the peptide is administered as a local anesthetic.

26. The method of claim 24, wherein the peptide is administered as an ocular anesthetic.

27. A method for characterizing a pore occlusion site on a sodium channel subtype
5 comprising determining the affinity of said site for a peptide of claim 1.

28. The method of claim 27, wherein said sodium channel subtype is a neuronal sodium
channel subtype and said peptide is μ -conopeptide S3.2 comprising an amino acid
sequence as set forth in SEQ ID NO:211 or SEQ ID NO:432.

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29. A method for screening a small molecule library to identify a small molecule which is a
selective blocking agent of a sodium channel subtype comprising (a) measuring the
blocking activity of a small molecule on said sodium channel subtype, (b) measuring the
blocking activity of a peptide of claim 1 on said sodium channel subtype and (c)
comparing the blocking activity of said small molecule with the blocking activity of said
peptide.

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30. The method of claim 29, wherein said sodium channel subtype is a neuronal sodium
channel subtype and said peptide is μ -conopeptide S3.2 comprising an amino acid
sequence as set forth in SEQ ID NO:211 or SEQ ID NO:432.

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31. A method for screening a small molecule library to identify a small molecule which is a
selective blocking agent of a sodium channel subtype comprising (a) measuring the
binding affinity of a small molecule on said sodium channel subtype, (b) measuring the
binding affinity of a peptide of claim 1 on said sodium channel subtype and (c)
comparing the binding affinity of said small molecule with the binding affinity of said
peptide.

32. The method of claim 31, wherein said peptide is radiolabeled.

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33. The method of claim 31, wherein said sodium channel subtype is a neuronal sodium channel subtype and said peptide is μ -conopeptide S3.2 comprising an amino acid sequence as set forth in SEQ ID NO:211 or SEQ ID NO:432.

5 34. The method of claim 33, wherein said peptide is radiolabeled.

10 35. A method for screening a small molecule library to identify a small molecule which is a selective blocking agent of a sodium channel subtype comprising (a) allowing a peptide of claim 1 to bind to a sodium channel subtype, (b) adding a small molecule and (c) measuring the amount of displacement of said peptide on said sodium channel subtype by said small molecule.

15 36. The method of claim 35, wherein said peptide is radiolabeled.

20 37. The method of claim 35, wherein said sodium channel subtype is a neuronal sodium channel subtype and said peptide is μ -conopeptide S3.2 comprising an amino acid sequence as set forth in SEQ ID NO:211 or SEQ ID NO:432.

25 38. The method of claim 37, wherein said peptide is radiolabeled.

39. A method for screening a small molecule library to identify a small molecule which is a selective blocking agent of a sodium channel subtype comprising (a) allowing a small molecule to bind to a sodium channel subtype, (b) adding a peptide of claim 1 and (c) measuring the amount of displacement of said small molecule on said sodium channel subtype by said small peptide.

30 40. The method of claim 39, wherein said sodium channel subtype is a neuronal sodium channel subtype and said peptide is μ -conopeptide S3.2 comprising an amino acid sequence as set forth in SEQ ID NO:211 or SEQ ID NO:432.

41. A method of identifying compounds that mimic the therapeutic activity of a μ -conotoxin, comprising the steps of: (a) conducting a biological assay on a test compound to

determine the therapeutic activity; and (b) comparing the results obtained from the biological assay of the test compound to the results obtained from the biological assay of a μ -conotoxin, wherein said μ -conotoxin is a peptide of claim 1.

5 42. The method of claim 41, wherein said μ -conotoxin is S3.2 comprising an amino acid set forth in SEQ ID NO:211 or SEQ IN NO:432.